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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,625	03/21/2007	Derek O'Hagan	PP020407.0004	7269

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,625	O'HAGAN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *21,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20, 22-26, and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/2/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-29 are pending in the application.

Election/Restrictions

2. Applicant's election of Group I, and the species wherein the polymer is a poly(α-hydroxy acid) (esp. poly(D,L-lactide-co-glycolide), and wherein the adjuvant is an oil-in-water emulsion in the reply filed on June 8, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 21, 27, and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species or invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 8, 2009.

4. Claims 1-20, 22-26, and 29 are under consideration.

Priority

5. It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/465841, filed April 25, 2003.

A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a).

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, a petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

In the present case, as reference to the priority application was made in the Declaration, and as the priority claim was recognized in the filing receipt, no petition under 37 CFR 1.78(a) is required.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on September 2, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

7. The objection to the specification made in the restriction requirement of April 2009 is withdrawn.

Claim Objections

8. Claims 1, 2, 6-8, 14, 15, and 22 are objected to because of the following informalities: these claims refer to Figures 2A-2C of the specification. Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. MPEP § 2173.05(s). It is suggested that the claims be amended to refer to the relevant positions of SEQ ID NO: 2 rather than the sequence of the indicated Figures.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 29 provides for the use of "use of a composition according to any of claims 1-6," but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 29 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 3-5, 7, 9-20, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to compositions (and methods of use thereof) comprising the administration of a HCV immunogen comprising an HCV E1E2 complex having at least 80% identity to positions 192-809 of Figure 2 (i.e. positions 20-637 of SEQ ID NO: 2).

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found

where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

As indicated above, the present claims are drawn to anti-HCV immunogenic compositions (and methods of using such) that include an E1E2 antigen wherein the antigens have any sequence with at least 80% sequence identity to positions 192-809 of Figures 2A-2C (i.e. SEQ ID NO: 2). Because the claims identify the sequences of SEQ ID NO: 4 as HCV antigens, they implicitly require that the claimed antigens are capable of inducing an immune response against a Hepatitis C virus. Thus, the claims read on a genus of antigens identified both by a generic structure, and a function.

In support of the specification, the application discloses only one member of the claimed genus, that of SEQ ID NO: 2. This single example represents a sequence of a known HCV isolate. Cf., SEQ ID NO: 4 to residues 192-809 of the HCV sequence disclosed in Choo et al., PNAS 88: 2451-55 (of record in the June 2006 IDS). With respect to sequences other than SEQ ID NO: 4, it is noted that the prior art teaches numerous HCV sequences, many of which presumably fall within the range of the indicated sequence identity. However, it is noted that not every sequence with 80% identity is an HCV sequence. Nor does the application identify any particular structure(s) within the indicated regions that are sufficient in themselves to induce an anti-HCV response. . It is not clear from the application what structures, residues, or regions in the claimed sequences must be maintained for the compositions to induce an anti-HCV response. I.e., there has been no showing of any structure that corresponds to the required functional characteristics of the claimed genus.

The teachings in the art indicate that single amino acid changes can alter the antigenicity of the protein. See e.g., Riffkin et al., Gene 167:279-83, abstract (indicating that a single amino acid change between two proteins determines the ability of such proteins to bind to an antibody). The art also indicates that amino acid substitutions outside of an antigenic site in a protein may affect that ability of the protein to react with antibodies targeting the protein. Abaza et al., J Prot Chem 11:433-44. Such uncertainty also applies to T-cell epitopes. See e.g., Gould et al., Semin Cell Dev Biol 9:321-28, esp. at pages 322-23. Thus, the art indicates that there is uncertainty in the ability of mutant versions of proteins to interact with or induce immune responses directed against the original protein. Thus, these teachings indicate that disclosure of a single sequence that may be an anti-HCV immunogen is not adequately representative of any sequence of at least 80% identity to that sequence which retains the functional characteristics of an anti-HCV immunogen.

Thus, while the teachings of the prior art and the application may provide support for compositions wherein the HCV antigens have the sequence of the indicated regions of SEQ ID NO: 4, or corresponding regions of other HCV isolates, the application has not provided sufficient support for any sequence of at least 80% identity with SEQ ID NO: 2 that would be able to induce an anti-HCV immune response.

13. Claims 7-20 and 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for the induction of an immune response against HCV through the practice of the claimed methods, does not reasonably provide enablement for methods for the therapy of HCV through such methods. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

In the present case, each of the claimed methods relates to the administration of an immunogenic composition comprising a cationic microparticle with a polynucleotide encoding an immunogenic HCV E1E2 complex adsorbed thereto, wherein the compositions are administered in "a therapeutically effective amount." It is noted that the specification does not provide a specific definition for "a therapeutically effective amount." However, on page 25 (lines 5-8), the application indicates that the terms “an effective amount” or “a pharmaceutically effective amount” may refer to amounts sufficient to induce an immunological response “and optionally, a corresponding therapeutic effect.” In lines 24-26 of the same page, the application defines the term treatment to include "the reduction or elimination of symptoms of the disease of interest (therapy)." Thus, the application appears to indicate that a therapeutic response would be one that is effective for the treatment of the disease, and therefore that a "therapeutically

effective amount" of the compositions in the claimed methods would therefore be effective for the treatment of HCV. The claims therefore read on methods for the treatment of HCV comprising the administration of the indicated compositions.

The present claims are drawn to hepatitis C virus vaccines comprising indicated HCV epitopes. Because the claims read on HCV vaccines, they implicitly require that the claimed compositions be enabled as providing an effective therapeutic or prophylactic benefit against HCV. In support of the claimed inventions, the application identifies a number of HCV epitopes, and indicates that those in the art would be capable of using such to induce anti-HCV immune responses, including anti-HCV T-cell responses. However, the application does not teach that the claimed compositions were capable of providing a therapeutic benefit against HCV infection.

The application teaches that the disclosed peptides were capable of inducing effective immune responses in animals, and therefore concludes they would be an effective agent in an anti-HCV vaccine.

However, the teachings in the art do not support the application's conclusion. In fact, the art teaches that, to date, there are no prophylactic or effective therapeutic treatments against HCV infection. See e.g., Rollier et al. (J Virol 78: 187-96, page 187); and Huang et al. (Antivir Res 71: 351-62, at 351) (each teaching that there are currently no anti-HCV vaccines, and that the most effective treatments involve compositions not comprising HCV antigens). These references teach that despite years of attempts to develop such a vaccine, those in the art have been hampered from doing so by several difficulties. See e.g., Rollier, at 187; and Berzofsky et al., J Clin Invest 114: 450-62, at 450 and 456-57. See also, Manns et al., Nat Rev Drug Discov 6:991-1000, at page 993. The Manns reference also notes the failure to achieve and effective

vaccine, despite also noting successes during the past decade of several instances where protective responses were noted in other animal models. Id. Thus, the art indicates that, despite years of studying the virus and attempting to make vaccines against it, and despite the development of compositions capable of inducing immune responses in animals, there has been no successful development of an anti-HCV vaccine.

Further, the failure to develop HCV vaccines and therapies have occurred despite the abundance of references through the past 10 years teaching the efficacy of HCV antigens in eliciting humoral and cellular immune response in several infection models. See e.g., Shirai et al., J Virol, 68: 3334-42; and Koziel et al., J Virol, 67: 7522-32.While other teachings in the art indicate that therapeutic vaccines have at least made it to clinical trials, such vaccines are generally protein or peptide based, have achieved variable results, and such results have been referenced as evidence of need to improve understanding of the interactions of HCV and human immune systems in the development of HCV vaccines. Stoll-Keller, Exp Rev Vaccines, 8:333-45, at page 341. Thus, the teachings in the art indicate significant difficulty and problems being faced by those in the art, and an as yet limited understanding in the field of the factors required for an effective anti-HCV vaccine, whether therapeutic or prophylactic.

It is also noted that each of the experiments described in the present application relate to the use of animal models. While the teachings in the art indicate that animal models are useful, at present there does not appear to be any established correlation between such models and effective therapy of HCV in humans. See e.g., Stoll-Keller, page 340 (noting differences in the chimp model, and indicating that definite conclusions on efficacy require human studies). Thus,

such models fail to provide adequate enabling support for the use of such vaccines in the main target of the HCV virus and of anti-HCV vaccines- humans.

In view of these teachings in the art relating to the difficulties and limited understanding of the art, the unpredictability in the art, and the limited teachings in the application with respect to the in vivo and therapeutic activity of the disclosed compositions, the application has not provided sufficient information to enable those in the art to treat and HCV infection with the claimed compositions. Because the compositions do appear to be immunogenic, the method claims are rejected as exceeding the scope for which they are enabled (i.e. they are rejected to the extent that they read on therapeutic uses of the compositions, rather than merely the induction immunogenic responses).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-11 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Houghton et al. (WO 01/47551) and of Choo et al. (PNAS 88:2451-55) (each of record in the restriction requirement mailed in April 2009). Claims 1-11 and 29 are drawn to compositions comprising a polynucleotide encoding an immunogenic HCV E1E2 complex, such as that represented by positions 20-637 of SEQ ID NO: 2 (and corresponding to residues 192-

809 of the HCV polyprotein sequence disclosed by Choo), wherein the polynucleotide is adsorbed onto a cationic microparticle. The dependent claims specify that the microparticle is formed from a poly(α-hydroxy acid) such as poly(D,L-lactide-co-glycolode) (PLG), and methods of using such to stimulate an immune response through the administration of the compositions to a subject.

Houghton teaches compositions for the induction of anti-HCV immune responses comprising HCV E1E2 complexes, or polynucleotides encoding such, and the induction of anti-HCV immune responses through the administration of the compositions. See abstract. The reference teaches that such polynucleotides may be administered through adsorption to a cationic microparticle, such as one made from PLG. Pages 22 and 39-40 (Example 4). The reference indicates that the polynucleotide may include control elements. Pages 10-11. However, it is noted that, while the reference suggests the use of polynucleotides encoding an E1E2 complex comprising the region of positions 192-809 of an HCV polyprotein (page 2, lines 24-29), the reference does not disclose a specific embodiment of such a sequence. The reference Houghton reference, alone, therefore does not teach or suggest a sequence sharing at least 80% homology to positions 192-809 of Figure 2 (i.e. residues 20-637 of SEQ ID NO: 2).

Positions 192-809 of the HCV polyprotein disclosed by Choo (page 2452, Figure 1) are identical the sequence presented in positions 20-637 of SEQ ID NO: 2. As the teachings of Houghton indicate that any corresponding HCV sequence may be used, and as Choo discloses an HCV polyprotein sequence, it would have been obvious to those of ordinary skill in the art to have used the sequence of Choo as the HCV sequence for use in the compositions suggested by

Houghton. The combined teachings of these references therefore render the claimed invention obvious.

16. Claims 1, 37, 9-11 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy et al. (WO 96/20698) in combination with the teachings of Selby et al. (U.S. 6,121,020) and of Felgner et al. (J Biol Chem 269:2550-61) and Liu et al. (Pharm Res 131856-60).

The Levy reference teaches microparticles complexed with an antigen such as those claimed in the present application. See e.g., pages 6-9. The reference teaches that the bioactive agents, including adjuvants and antigens (pages 8 and 10, may be incorporated into, or adsorbed onto the particle (page 15, second paragraph). The document also teaches that surfactants and detergents may be incorporated into the particle (page 15, first paragraph), and indicates that such incorporation helps with the incorporation or attachment of the bioactive agent (e.g. page 16, second full paragraph). From the teachings of Levy, it would appear that the described methods of incorporating the polynucleotides into the microspheres would inherently result in the adsorption of at least some of the polynucleotides onto the surface of the resulting particles. The reference also teaches that the antigen may be an antigen such as used in a DNA vaccine (page 11, carryover paragraph from page 10). The reference also indicates that the antigens of the invention may be Hepatitis Viral components, or DNA-based vaccines. Pages 10-11. Thus, the reference suggests microparticles comprising DNA-based vaccines for the induction of immune responses.

Further, each of Felgner and Liu teaches the use of cationic liposomes for the delivery of nucleic acids for expression. Liu indicates that such means for the delivery of DNA were desired

as an alternative to viral-based vectors. Felgner teaches the making of cationic liposomes to which DNA plasmids are adsorbed due to the opposite charges of the liposome and the DNA. Page 2550 (right column) and page 2551. Each of the references indicates that, while the complexes were successful for the delivery of the DNA, problems remain with the use of these complexes. Thus, these references indicate that DNA may be successfully delivered to cells through complexing with cationic based agents, including through surface complexing (i.e. adsorption) to cationic liposomes. The references indicate that it is the cationic charge of the liposomes that enables the liposome to adsorb to the target DNA.

From these teachings, it would have been obvious to those of ordinary skill in the art to have modified the particles of Levy for the delivery of DNA in a similar manner. As Levy teaches that the particles may be formed to both include adsorbed bioactive agents, and detergents of various charges, it would have been obvious to those of ordinary skill in the art that DNA plasmid could be adsorbed to the surface of such particles through the incorporation of cationic molecules into the particle so as to make a particle with a cationic charge.

However, it is also noted that none of the previously described references in this rejection identify the E1E2 antigen, or the specifically encoded E1E2 antigen of the present claims. Selby teaches anti-HCV immunogenic compositions comprising truncated E1E2 complexes or polynucleotides encoding such. Abstract, columns 11-12. It is noted that the combined HCV E1E2 sequences disclosed in SEQ ID NOs: 3 and 4 of the patent are identical to amino acids 20-637 of SEQ ID NO: 2. However, as the reference teaches deletions from these sequences (see e.g., claims 1-3) the resulting E1E2 complex would contain amino acid sequences that share only 80% identity with SEQ ID NO: 2.

From these teachings, it would have been obvious to those of ordinary skill in the art to have made microparticles as suggested by Levy, Felgner, and Liu which comprise as the polynucleotide encoding the antigen a polynucleotide encoding the E1E2 complex described by Selby. The combined teachings in the art therefore render the claimed inventions obvious.

17. Claims 12-20 and 22-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Houghton and Choo as applied to claims 1-11 and 29 above, and further in view of Ertl (U.S. 6,210,663). These claims are . Claims 12-20 and 22-26 read on the methods of using the compositions, further comprising later administration of a second amount of a composition comprising an HCV polypeptide antigen wherein the second composition may additionally be formulated with an adjuvant, such as the oil-in-water formulation of (e.g.) claims 19 and 20.

The teachings of Houghton and Choo have been described in part above. The Houghton reference also suggests the administration of multiple doses of the compositions (page 32), and the inclusion of adjuvants with the polypeptide E1E2 compositions, such as the oil-in-water formulations described by (e.g.) claims 17-20 (page 25, lines 3-18.. In addition, the teachings of Ertl specifically suggest the administration of a polypeptide composition after the prior administration of a DNA encoding the polypeptide. Abstract, columns 12-13. It would therefore have been obvious to those of ordinary skill in the art to have combined such teachings so as to arrive at the presently claimed methods. The combined teachings of the prior art therefore render the indicated claims obvious.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 1-20, 22-26, and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of U.S. Patent No. 7,329,408 in view of the teachings of Houghton, Choo, and Ertl as applied above. Although the conflicting claims are

not identical, they are not patentably distinct from each other because the primary difference between the present methods and those of the patent are that the patent claims do not specify that the polynucleotide is adsorbed to a microparticle, or the sequence of the HCV E1E2 complex encoded by the polynucleotide. However, it is noted that the only example of the use of PLG particle in the patent specification relates to the use of a polynucleotide adsorbed to the surface of the particle. See e.g., Example 4. It is also noted that the patent claims do not specifically teach or suggest the additional administration of the second composition of (e.g.) claim 12. Moreover, this and the other missing limitations are suggested by the secondary references as described in the obviousness rejections above.

21. Claims 1-20, 22-26, and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-42 and 62-76 of copending Application No. 10/775964, or over claims 1-3, 5, 6, 9, 10, 12, 13, 15-17, 23, 26-28, 32-35, 37-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76, 77, 79-81, 83, and 87-101 of copending application 10/757708, in view of Houghton, Choo, and Ertl as applied above. The copending claims of '964 application are drawn to methods of making microparticles of a poly(α-hydroxy acid) such as PLG as a carrier for a macromolecule such as a polynucleotide, wherein the resulting particle may be a cationic particle with the polynucleotide adsorbed to the surface thereof, and to the resulting particles. The claims of '708 application further indicate that the polynucleotides may encode HCV antigens (claim 17), and teach methods for inducing an immune response with such particles. The copending claims are silent as to the presence of the specific polynucleotides of the present claims, the administration of the second composition, and

the presence of the adjuvant. However, such would have been obvious from the teachings of the previously applied Houghton, Choo, and Ertl references.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims. In the present case, the copending applications are divisionals of the current application or any parent or child thereof, and the specifications of the copending applications suggest the use of the disclosed particles for the induction of immune responses. The present claims are therefore would have been obvious from the teachings of the copending claims alone, or in combination with Houghton, Choo, and Ertl.

This is a provisional obviousness-type double patenting rejection.

22. Claims 1-20, 22-26, and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 12, 13, 15-38, 41, 45-48, 51, 52, 55-71, 76, and 77 of copending Application No. 11/653792 in view of Houghton, Choo, and Ertl as applied above. The copending claims read on compositions comprising polynucleotides adsorbed to a microparticle such as is described by the present claims, and wherein the polynucleotide may encode an antigen, such as an HCV antigen. The copending claims teach methods of making and using such particles, including methods for the induction of

an immune response against the encoded antigens. While the copending claims are silent as to the encoded HCV antigen, and as to the administration of a second effective amount of the composition, and the oil-in-water adjuvant, such would have been obvious from the teachings of the previously applied art (Houghton, Choo, and Ertl). The present claims are therefore obvious embodiments of the copending claims.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims. In the present case, the copending application is not a divisional of the current application or any parent or child thereof.

This is a provisional obviousness-type double patenting rejection.

23. Claims 1-20, 22-26, and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 12/231351; or claims 117, 22-33, 36-40, and 55-62 of copending application 12/087330; in view of Houghton, Choo, and Ertl as applied above. The copending claims read on immunogenic compositions comprising polynucleotides encoding HCV E1E2 complexes. The copending claims of the '351 application are silent as to the adsorption of the polynucleotides to a microparticle such as is described by the present claims, as to the sequence of the encoded

HCV antigen, and as to the administration of a second effective amount of the composition, and the oil-in-water adjuvant. The copending claims of the '330 application are silent as to the adsorption of the polynucleotides to a microparticle such as is described by the present claims, and as to the administration of a second effective amount of the composition. However, such would have been obvious from the teachings of the previously applied art (Houghton and Choo). The present claims are therefore obvious embodiments of the copending claims.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims. In the present case, the copending applications are not divisionals of the current application or any parent or child thereof.

This is a provisional obviousness-type double patenting rejection.

24. Claims 1-20, 22-26, and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5, 6, 9-12, 15-24, 26-31, 35-44, and 46-50 of U.S. Patent No. 6,884,435; or over claims 1-13, 15-17, 20, and 24-51 of US Patent No 6,753,015; in view of Houghton, Choo, and Ertl.

The '435 patent claims read on microparticles such as those described in the present claims with polynucleotides encoding antigens, such as HCV antigens, adsorbed on the surface

thereof, and methods of using such for the induction of an immune response. While the patent claims do describe the encoded HCV antigen, and as to the administration of a second effective amount of the composition, and the oil-in-water adjuvant, such would have been obvious from the teachings of the previously applied art (Houghton and Choo). The present claims are therefore obvious embodiments of the patent claims.

The '015 patent claims read on microparticles such as those of present claims with polynucleotides encoding antigens, such as HCV antigens, adsorbed on the surface thereof, and methods of using such for the induction of an immune response, or for making such particles. While the patent claims do describe the encoded HCV antigen, and as to the administration of a second effective amount of the composition, and the oil-in-water adjuvant, such would have been obvious from the teachings of the previously applied art (Houghton and Choo). The present claims are therefore obvious embodiments of the patent claims.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims. In the present case, the patents are not divisionals of the current application or any parent or child thereof.

Conclusion

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648